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File No. ST96016-US

THE UNITED STATES PATENT AND TRADEMARK OFFICE

#11 B.J 7/21/00

In re Patent Application of: Pierre Wils et al. Group Art Unit: 1636

Serial No.: 09/153,838 Examiner: J. Ketter

Filing Date: September 15, 1998

For: PURIFICATION OF PLASMID DNA OF PHARMACEUTICAL QUALITY

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this paper (along with any referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Box AF, Assistant Commissioner for Patents, Washington, D.C. 20231.

Joyce C. Lynch
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To: Box AF
Assistant Commissioner For Patents
Washington, D.C. 20231

APPELLANTS' BRIEF

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This brief and its appendices are transmitted in triplicate.

The requisite fee is submitted herewith. Please credit any overpayment or charge any deficiency to Deposit Account No. 18-1982.

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The present application is assigned to Rhône-Poulenc Rorer S.A., having its principal place of business at 20 Avenue Raymond Aron, Antony Cedex 92165 France. Accordingly, Rhône-Poulenc Rorer S.A. is the real party in interest.

2. RELATED APPEALS AND INTERFERENCES

The appellants, assignee and the legal representative of both are unaware of any other appeal or interference which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

3. STATUS OF CLAIMS

a. Claims cancelled: 23 and 24.

b. Claims withdrawn from consideration but not cancelled: none.

c. Claims pending: 1-22, 25 and 26.

d. Claims allowed: 1-22.

e. Claims rejected: 25 and 26.

f. Claims appealed: 25 and 26.

Appealed claims 25 and 26 as currently pending are attached as Appendix A hereto. Allowed claims 1-22 are attached as Appendix B hereto.

4. STATUS OF AMENDMENTS

An amendment was filed October 12, 1999, after the Final Action of August 17, 1999. The Examiner indicated that that amendment, by virtue of which appealed claims 25 and 26 were amended to read as set forth in Appendix A and claims 23 and 24 were cancelled, would be entered upon filing of a Notice of Appeal.

5. SUMMARY OF THE INVENTION

The invention as claimed in claims 25 and 26 is directed to a composition comprising DNA that has been purified by the process of allowed claim 1, and a pharmaceutically acceptable carrier, the purified DNA having a chromosomal DNA content less than or equal to 0.01% and an endotoxin content less than or equal to 50 EU/mg. (Claim 25 specifies a preferred endotoxin upper limit of 10 EU/mg.) There is no suggestion or expectation in the prior art cited by the Examiner of purified DNA having the characteristics recited in claims 25 and 26, much less to a composition comprising such DNA and a carrier.

6. ISSUE

Are claims (25 and 26) to a composition comprising purified DNA having a chromosomal DNA content of 0.01% or less and an endotoxin content of 50 EU/mg or less, produced by the process of allowed claim, which employs a purification step of ceramic hydroxyapatide column chromatography, inherently anticipated by the disclosures of either of two cited references, neither of which discloses either the ceramic hydroxyapatide column chromatography purification step or purified DNA having the above-recited purity characteristics?

7. GROUPING OF CLAIMS

Claims 25 and 26 are patentably distinct in that claim 25 further limits the endotoxin content of the claimed purified recombinant plasmid DNA composition of claim 26 to 10 EU/mg or less.

Independent claim 26 recites that the DNA of the claimed purified DNA composition has a chromosomal DNA content of 0.01% or less and an endotoxin content of 50 EU/mg.

8. ARGUMENT

A. The Examiner has improperly rejected claims 25 and 26 based on alleged anticipatory inherent disclosure of the subject matter thereof by either Woodward et al. (U.S. Patent No. 5,674,997) or Horn et al. (U.S. Patent No. 5, 576,196).

1. The Examiner failed to establish a prima facie case that claims 25 and 26 are anticipated by the prior art.

Woodward et al. are concerned only with methods of purifying DNA by separating it from other cellular materials using silicon-containing material. However, the patentees do not even mention the separation of chromosomal DNA from plasmidic DNA. They do not disclose a pharmaceutical grade product and are silent about the endotoxin or chromosomal DNA content. They not only fail to disclose or suggest the process described and claimed in the present application, they also fail to disclose DNA products having the attributes recited in product claims 25 and 26.

Horn et al. disclose a process for reducing RNA concentration in a mixed solution of RNA and DNA by using diatomaceous earth. However, as is the case of Woodward et al. discussed above, Horn et al. also fail to disclose or suggest either the process of claim 1 or DNA compositions having the attributes recited in claims 25 and 26. In particular, Horn et al., teach nothing about separating chromosomal DNA from plasmid DNA (both of which generally travel together). Therefore, there is no basis whatever for the Examiner's conclusion the the product of the Horn et al. procedure would inherently have the low chomrosomal DNA content recited in claim 26. Thus, even if the endotoxin content of their product were within the 50 EU/mg limitation recited in claim 26, the Horn et al. disclosure still fails to suggest, much less anticipate, the purified, low chromosomal DNA content composition recited in claim 26. A fortiori, the lower endotoxin content composition recited in dependent claim 25 is nowhere suggested or anticipated by Horn et al.

The Examiner merely makes the unsupported conclusion that, since the cited references are concerned with purifying DNA, their products must inherently have the purity recited in claims 25 and 26. However, it is well established that, in order to support anticipation rejections based on inherency, the Examiner must show factual and technical reasons that establish that the allegedly inherent feature necessarily flows from the teaching of the prior art. Ex parte Levy, 17 U.S.P.Q. 2d 1461, 1464 (Bd. Pat. App. & Int. 1990). Thus, the fact that the prior art composition could possibly have the same features as the claimed invention will not support a finding of inherency. Rather, the inherency must flow as a necessary conclusion from the prior art, not simply a possible one. In re Oebrich, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981) (emphasis added).

Accordingly, the Examiner has failed to establish a prima facie case of anticipation, and the Board is respectfully requested to reconsider and reverse the rejection of claims 25 and 26 as anticipated by either Woodward et al. or Horn et al. (the only rejection of these claims in the Final Action).

9. CONCLUSION

In view of the above, it is submitted that the claims of the present application are in condition for allowance, and a decision to that effect is respectfully requested.

Respectfully submitted,

Dated: 7/13/00

Irving Newman
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APPENDIX A

25. The purified recombinant plasmid DNA composition according to claim 26, wherein the content of endotoxin is less than or equal to 10 EU/mg.

26. A composition comprising DNA obtained by the process of claim 1 and a pharmaceutically acceptable carrier, wherein said DNA has a chromosomal DNA content that is less than or equal to 0.01%, and an endotoxin content that is less than or equal to 50 EU/mg.

APPENDIX B

1. In a process for purifying double-stranded DNA comprising lysing cells followed by one or more chromatographic separation steps, the improvement comprising separating the DNA from other biological material in admixture therewith using ceramic hydroxyapatite column chromatography.

2. A process according to claim 1 for purifying double-stranded DNA, comprising using two chromatographic steps, of which one is ceramic hydroxyapatite column chromatography.

3. The process according to claim 2, further comprising using affinity chromatography or ion exchange chromatography.

4. The process according to claim 3, wherein the affinity chromatography involves triple helix formation between the DNA and an immobilized oligonucleotide.

5. The process according to claim 3, wherein the ion exchange chromatography is anion exchange chromatography.

6. The process according to claim 1, further comprising a step of diafiltration.

7. The process according to claim 2, further comprising a step of diafiltration.

8. The process according to claim 3, further comprising a step of diafiltration.

9. The process according to claim 4, further comprising a step of diafiltration.

10. The process according to claim 5, further comprising a step of diafiltration.

11. A process for purifying double-stranded DNA, comprising

chemical lysing of cells,

diafiltration,

using ceramic hydroxyapatite column chromatography, and

using affinity chromatography involving triple helix formation between the DNA and an immobilized oligonucleotide.

12. The process according to claim 1, wherein the double-stranded DNA is a plasmid.

13. The process according to claim 2, wherein the double-stranded DNA is a plasmid.

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16. The process according to claim 5, wherein the double-stranded DNA is a plasmid.

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18. The process according to claim 7, wherein the double-stranded DNA is a plasmid.

19. The process according to claim 8, wherein the double-stranded DNA is a plasmid.

20. The process according to claim 9, wherein the double-stranded DNA is a plasmid.

21. The process according to claim 10, wherein the double-stranded DNA is a plasmid.

22. The process according to claim 11, wherein the double-stranded DNA is a plasmid.

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Independent claim 26 recites that the DNA of the claimed purified DNA composition has a chromosomal DNA content of 0.01% or less and an endotoxin content of 50 EU/mg.

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The Examiner merely makes the unsupported conclusion that, since the cited references are concerned with purifying DNA, their products must inherently have the purity recited in claims 25 and 26. However, it is well established that, in order to support anticipation rejections based on inherency, the Examiner must show factual and technical reasons that establish that the allegedly inherent feature necessarily flows from the teaching of the prior art. Ex parte Levy, 17 U.S.P.Q. 2d 1461, 1464 (Bd. Pat. App. & Int. 1990). Thus, the fact that the prior art composition could possibly have the same features as the claimed invention will not support a finding of inherency. Rather, the inherency must flow as a necessary conclusion from the prior art, not simply a possible one. In re Oebrich, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981) (emphasis added).

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APPENDIX A

25. The purified recombinant plasmid DNA composition according to claim 26, wherein the content of endotoxin is less than or equal to 10 EU/mg.

26. A composition comprising DNA obtained by the process of claim 1 and a pharmaceutically acceptable carrier, wherein said DNA has a chromosomal DNA content that is less than or equal to 0.01%, and an endotoxin content that is less than or equal to 50 EU/mg.

APPENDIX B

1. In a process for purifying double-stranded DNA comprising lysing cells followed by one or more chromatographic separation steps, the improvement comprising separating the DNA from other biological material in admixture therewith using ceramic hydroxyapatite column chromatography.

2. A process according to claim 1 for purifying double-stranded DNA, comprising using two chromatographic steps, of which one is ceramic hydroxyapatite column chromatography.

3. The process according to claim 2, further comprising using affinity chromatography or ion exchange chromatography.

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In re Patent Application of:	Pierre Wils et al.	Group Art Unit: 1636
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APPENDIX A

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